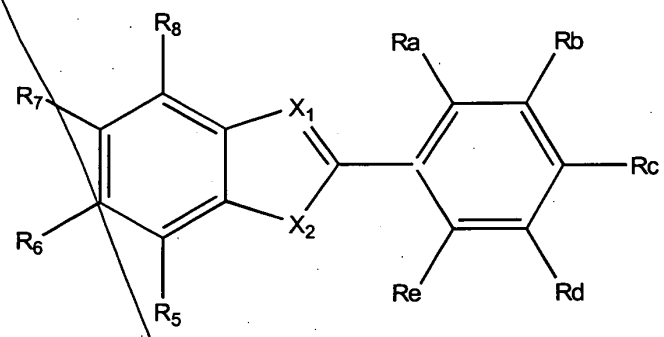
Claims

1. A compound of formula (I)(B):



wherein

X_1 is CR_1, wherein R_1 is H, halo, cyano, amino, or nitro; and X_2 is NR_3;

R_3 is H, $-SO_2$ (C_{1-6} alkyl), $-SO_2$ phenyl, (C=O)(C_{1-6} alkyl), or -W'Z';

W' is a covalent bond, (C=O), SO_2, or C_{1-6} alkyl;

Z' is C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, phenyl, or C_{2-6} heterocyclic radical, optionally including in the ring up to 3 additional heteroatoms or moieties independently selected from O, N, NH, S, SO, and SO_2; or Z' is $NR_{13}R_{14}$ where each of R_{13} and R_{14} is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical;

each of R_5, R_6, R_7 and R_8 is independently H, C_{1-6} alkyl, C_{1-6} alkoxy, halo, nitro, or amino;

one of R_a, R_b, R_c, R_d, and R_e is WZ and the others are independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, halo, nitro, and amino;

W is -O-, R_9, O-R_9, NR_{10}, -(CO)(O)R_9, -O (CO)R_9, -(CO)NR_{10}, or -N(R_{10})-CO-R_9, wherein R_9 is C_{1-6} alkylene, C_{2-6} alkynylene, C_{2-6} alkenylene, phenylene, or C_{2-5} heterocyclic bivalent radical, and R_{10} is H, C_{1-6} alkyl, C_{2-6} alkynyl, C_{2-6} alkenyl, phenyl, or C_{2-5} heterocyclic radical;

Z is C_{2-8} heterocyclic radical with at least one basic nitrogen atom in the ring, optionally including in the ring up to 3 additional

heteroatoms or moieties independently selected from O, C=O, N, NH, NG, S, SO, and SO_2, wherein G is R_{15}, COR_{15}, $COOR_{15}$, SO_2R_{15}, SO_2N, CSR_{15}; or Z is $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-6} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; or $NR_{11}R_{12}$ taken together is a C_{6-8} cycloalkylimino radical; and R_{15} is C_{1-6} alkyl, C_{2-6} alkynyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, and C_{4-7} cycloalkenyl; each of the above hydrocarbyl or heterocyclic groups being optionally substituted with between 1 and 3 substituents selected from C_{1-3} alkyl, C_{1-3} alkoxy, halo, hydroxy, phenyl, and phenyl(C_{1-3} alkyl); and wherein each of the above heterocyclic groups may be attached to the rest of the molecule by a carbon atom or a heteroatom;
or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

2. A compound of claim 1, wherein R_3 is H or C_{1-3} alkyl.

3. A compound of claim 1, wherein R_3 is -(C=O)C_{1-6} alkyl.

4. A compound of claim 1, wherein R_3 is -SO_2(C_{1-3} alkyl).

5. A compound of claim 4 wherein R_3 is methylsulfonyl.

6. A compound of claim 1, wherein W' is a covalent bond.

7. A compound of claim 1, wherein W' is SO_2 or (C=O).

8. A compound of claim 1, wherein R_c is WZ.

9. A compound of claim 1, wherein R_b or R_d is WZ.

10. A compound of claim 1, wherein W is ethoxy, propoxy, or butoxy.

11. A compound of claim 1, wherein W is -O-.

12. A compound of claim 1, wherein one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, nitro, and halo; and R_a and R_d are each independently H or methyl.

B' cont

13. A compound of claim 1, wherein at least two of the following apply: R_c is WZ; W is propoxy or ethoxy; and Z is N-piperidino, 2-(N-methyl)pyrrolidino, or N,N-dimethyl.

14. A compound of claim 1, wherein Z is pyrrolidino, N-methyl-pyrrolidino, pyridyl, thiazoyl, piperidino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-6} alkyl, phenyl, benzyl, C_{3-6} cycloalkyl, and C_{2-5} heterocyclic radical or taken together with the N form a C_{6-8} cycloalkylamino radical.

15. A compound of claim 1, wherein one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo; and R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, piperazino, N-methylpiperazino,or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; each of R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy; each of R_5 and R_8 is H.

16. A compound of claim 15, wherein R_3 is H or $-SO_2$ (C_{1-6} alkyl).

17. A compound of claim 15, wherein R_3 is SO_2(phenyl) and (C=O)(C_{1-6} alkyl).

18. A compound of claim 15, selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1H-indole, 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1-(methylsulfonyl) -1H-indole, and 2-[4-[3-Piperidinopropoxy]phenyl)-1H-indole;) 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

19. A compound of claim 15, selected from 2-[4-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole, and 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

20. A pharmaceutical composition comprising a compound of formula (I)B and a pharmaceutically acceptable carrier.

21. A pharmaceutical composition of claim 20, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

22. A pharmaceutical composition of claim 21, wherein said compound has a formula selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1H-indole; 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1-(methylsulfonyl) -1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

23. A method for treating disorders mediated by the histamine H_3 receptor in a patient, said method comprising administering to the patient a pharmaceutically effective amount of compound of formula (I)B.

24. A method of claim 23, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, N-methylpiperazino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

25. A method for treating a patient with a central nervous system disorder, said method comprising administering to the patient a pharmaceutically-effective amount of a compound of formula (I)B.

26. A method of claim 25, wherein said central nervous system disorder is selected from sleep/wake disorders, arousal/vigilance disorders, dementia, Alzheimer's disease, epilepsy, narcolepsy, eating disorders, motion sickness, vertigo, attention deficit hyperactivity disorder, learning and memory disorders, mild cognitive impairment, and schizophrenia.

27. A method of claim 25, wherein said disorder is selected from sleep/wake disorders, arousal/vigilance disorders, attention deficit hyperactivity disorder, and learning and memory disorders.

28. A method of claim 25, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, N-methylpiperazino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

29. A method of claim 25, wherein said compound has a formula selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]-phenyl)-1H-indole; 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]-phenyl)-1-(methylsulfonyl) -1H-indole; 2-[4-[3-Piperidino-propoxy]phenyl)-1H-indole; 2-[4-[3-Piperidinopropoxy]-phenyl)-1-(methylsulfonyl)-1H-indole; 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

30. A method for treating a patient with an upper airway allergic response, said method comprising administering to the patient a pharmaceutically-effective amount of a compound of formula (I)B.

31. A method of claim 30, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, N-methylpiperazino or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

32. A method of claim 30, wherein said compound has a formula selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1H-indole; 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1-(methylsulfonyl) -1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.